

Applicant: Arie Pieter Otte
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Amendments to the Claims:

Please cancel claims 26, 27 and 43 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or divisional application. Please amend claims 25, 28-30, 35-37 and 44-46, and add new claims 56-63 as set forth below.

1-24. (Canceled)

25. (Currently Amended) A method of detecting, and optionally selecting, a DNA sequence, wherein the DNA sequence to be detected possesses a stable expression-enhancing modulating quality, which method comprises the steps of:

- 1) cloning ~~in a vector of~~ DNA fragments into vectors at a location between i) a DNA sequence comprising a binding site for a repressor protein, which repressor protein is involved in the induction of gene-transcription repressing chromatin, and ii) a reporter gene comprising a promoter, resulting in a variety of fragment-comprising vectors;
- 2) introducing the vectors into ~~a transcription system~~ host cells; and
- 3) subjecting the host cells to a selection step in order to identify ~~the a~~ DNA sequence with a stable expression-enhancing modulating quality;

~~wherein the DNA sequence involved with the induction of gene transcription repressing chromatin binding site is a DNA sequence that is recognized by a heterochromatin binding repressor protein comprising a first part recognizing said binding site and a second part inducing formation of chromatin in which transcription is repressed, HP1, which HP-1 comprising complex repressor protein is present in the transcription system and/or the host cells.~~

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26-27. (Canceled)

28. (Currently Amended) A method according to claim 25, wherein the cloned DNA fragments have a size of fewer than 5,000 base pairs.

29. (Currently Amended) A method according to claim 25, wherein the distance between the ~~DNA sequence involved in gene repressing chromatin binding site~~ and the reporter gene is fewer than 5,000 base pairs.

30. (Currently Amended) A method according to claim 25, wherein the promoter may be active in the ~~transcription system~~ host cells but wherein induction of gene-repressing chromatin in the vectors results in the repression of transcription of the reporter gene.

31. (Previously presented) A method according to claim 25, wherein the selection in step 3) occurs by using a reporter gene which provides resistance to a growth inhibitor.

32. (Previously presented) A method according to claim 31, wherein the host cells are cultivated in the presence of the growth inhibitor.

33. (Previously presented) A method according to claim 32, wherein the growth inhibitor is present in a concentration sufficiently high to kill host cells in which the gene providing resistance to the growth inhibitor is not active.

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34. (Previously presented) A method according to claim 33, wherein an antibiotic is used as the growth inhibitor and the reporter gene provides resistance to the antibiotic.

35. (Currently Amended) A method according to claim 34 25, wherein the reporter gene codes for Green Fluorescent Protein.

36. (Currently Amended) A method according to claim 35 25, wherein the reporter gene is luciferase.

37. (Currently Amended) A method according to claim 36 35, wherein the fluorescent host cells are separated from non-fluorescent host cells by means of a Fluorescence-Activated Cell Sorter (FACS).

38. (Previously presented) A method according to claim 29, wherein the cloned DNA fragments have a size of substantially between 2,000-3,000 base pairs.

39-43. (Canceled)

44. (Currently Amended) A method according to claim 43 25, wherein the repressor protein complex comprises a fusion protein.

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45. (Currently Amended) A method according to claim 44, wherein the first part of the repressor protein is a part binding the DNA binding site of LexA-DNA or GAL4-DNA.

46. (Currently Amended) A method according to claim 25, wherein the organism DNA fragments in step 1) is are derived from the genome of selected from the group comprising a plant or and a vertebrate.

47. (Previously presented) A method according to claim 46, wherein the vertebrate is a mammal.

48. (Previously presented) A method according to claim 25, wherein the vector is an episomally replicating vector.

49. (Previously presented) A method according to claim 48, wherein the vector comprises a replication origin from the Epstein-Barr virus (EBV), OriP, and a nuclear antigen (EBNA1).

50-55. (Canceled)

56. (New) A method according to claim 34, wherein the antibiotic is zeocin.

57. (New) A method according to claim 25, wherein the host cells are human U-2 OS cells.

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58. (New) A method according to claim 25, wherein the promoter is the SV40 promoter.

59. (New) A method according to claim 25, wherein the second part of the repressor protein comprises heterochromatin-binding protein 1 (HP1).

60. (New) A method according to claim 25, wherein the second part of the repressor protein comprises a Polycomb-group (PcG) protein.

61. (New) A method according to claim 25, wherein the second part of the repressor protein comprises a protein having histone deacetylase activity.

62. (New) A method according to claim 25, wherein the second part of the repressor protein comprises methyl-CpG-binding protein 2 (MeCP2).

63. (New) A method according to claim 60, wherein the PcG protein is selected from the group consisting of HPC2, RING1, and Su(z)2.